REMARKS

Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

PENDING CLAIMS and AMENDMENTS THERETO

Claims 1, 2, 4, 5, 9, 10, 12, 16-19, 22-49 have previously been canceled without prejudice or disclaimer.

Claims 50-51 were submitted in Applicants' Amendment filed June 3, 2003 in response to the Final Office Action mailed April 24, 2003, but were not entered.

Claims 3 and 11 were amended and claims 52-53 were added in the Preliminary Amendment accompanying Applicants' request for Continued Examination (RCE), filed on July 24, 2003. Applicants bring to the Examiner's attention that, in keeping with 37 CFR 1.126, when new claims are presented, they are required to be numbered consecutively beginning with the number following the highest numbered claim previously presented, whether entered or not. Thus, though claims 50-51 were not entered, the next number for any subsequent new claim would be 52. Thus, any new claim subsequent to Applicants' response filed 6/3/03 would begin with claim 52. Therefore, it is Applicants' position, that claims 52-53, entered by amendment on July 24, 2003, are not misnumbered and hereby request the Examiner in the next communication from the Office to note for the record that Applicants numbering of claims 52-53 is correct.

Claims 13-15, 20, 21, 23 and 40-49 were withdrawn from consideration pursuant to Applicants' election of the claims of Group II in their Response to the Restriction Requirement mailed May 13, 2002, which response was filed on June 13, 2002. Simultaneously, Applicants also made a request for rejoinder of method of use claims 13-15, 20-21, and 49 (now canceled) under *In re Ochiai, In re Brouwer*, and 35 U.S.C. § 103(b).

Claim Objections

Applicants note that the Examiner has indicated that claims 50-51 [sic] (i.e., claims 52-53) would be allowable if rewritten in independent form. Applicants request that the Examiner's objection to claims 52-53 be held in abeyance pending consideration of Applicants' amendments and arguments.

Amendments Not Entered by the Examiner

In Applicants' Response to Final, filed June 3, 2003, Applicants attempted to amend subsection (d) of claim 3, directed to immunogenic fragments of SEQ ID NO:1, by adding the further limitations that the fragment is "of at least 5 amino acids" of SEQ ID NO:1, and that the "immunogenic fragment is used to make an antibody which specifically binds to an isolated polypeptide selected from the group consisting of a), b) and c)" of claim 3. Applicants also attempted to add new claims 50 and 51, directed, respectively, to a method of producing the polypeptides of claim 3, and to a method of producing the polypeptide comprising the amino acid sequence of SEQ ID NO:1.

The Advisory Action of July 8, 2003 indicated the Examiner's refusal to enter the Amendment After Final requested in the response filed June 3, 2003. The Examiner reasoned that adding new claims 50 and 51 would require further consideration and/or further searches, because they were directed to producing a polypeptide of claim 3 and claim 3 is directed to polynucleotides.

The amendment to claim 3(d), as requested in the Response filed June 3, 2003, would have overcome the written description rejection of claims 3 and 6-8 under 35 U.S.C. §112, first paragraph as to those [immunogenic] fragments and was so indicated by the Examiner (see Advisory Action mailed July 8, 2003, No. 3, pages 1-2). The identical amendment to claim 3(d) was requested in the Preliminary amendment filed with the RCE request on July 23, 2003. The Examiner has indicated that Applicants' submission filed on 7/25/03 has been entered (Office Action of August 29, 2003, page 2).

Therefore, claims 3, 6-8, 11, 13-15, 20-21 and 52-53 are currently pending.

Claims 3, 6-8, and 11, are currently under consideration in this application.

Rejoinder of Method Claims

The Final Rejections presented in the Final Office Action of April 24, 2003 indicated that claim 11 was directed to an allowable product, and that in light of the allowable product claim, claims 13-15 and 21, directed to methods of making and using the polynucleotides recited in claim 11 would be rejoined and examined pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86). Applicants assert that claim 20 (which depends from claim 53) should also properly be rejoined, as it too is a method of using the polynucleotide of claim 11, as evident by the dependency of claim 53 from claim 11.

Applicants reiterate that upon allowance of any of the product claims (claims 3, 6, 7, 11, 53), there should be rejoinder of "method of use" claims 8, 13-15, 20-21 and 52, in accordance with the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)."

Rejection under 35 U.S.C. §112, first paragraph, written description

Claims 3, 6-8 and 11 stand rejected under the first paragraph of 35 U.S.C. §112 for allegedly containing subject matter "not described in the specification in such a way as too reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." The Office Action asserts that:

- . . . the specification discloses an isolated cDNA sequence, SEQ ID NO:2, . . . (Office Action of August 29, 2003, page 4);

- . . . disclosure of a single species of nucleic acid dose not adequately describe the scope of the claimed genus, . . . The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides . . . (Office Action of August 29, 2003, page 4)

- . . . the specification as filed does not provide adequate written description support for a polypeptide having at least 90% sequence identity to SEQ ID NO:1 (Office Action of August 29, 2003, page 4);

  and

- Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of the specific nucleotide sequences and the ability to screen, is insufficient to describe the genus. (Office Action of August 29, 2003, page 5).

This rejection is respectfully traversed.

I. The Legal Standard

The requirements necessary to fulfill the written description requirement of 35 U.S.C. § 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

> . . . Mention of representative compounds encompassed by generic claim language ***clearly is not required by Section 112 or any other provision of the statute***. But, where no explicit description of a generic invention is to be found in the specification...mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]

> . . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, ***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'*** *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., ***complete or partial structure***, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. ***If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.*** [emphasis added] [footnotes omitted]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what

is conventional or well known to one skilled in the art.

A. The specification provides an adequate written description of the claimed "variants" of SEQ ID NO:2 and "variants" of SEQ ID NO:1

The subject matter encompassed by Claims 3 and 11 are either disclosed by the specification or conventional or well known to one skilled in the art.

At the outset it should be noted that: 1) SEQ ID NO:2 encodes SEQ ID NO:1, 2) SEQ ID NO:1 (PDE9A) is a new member of the cyclic phosphodiesterase family of proteins, and 3) SEQ ID NO:1 has cyclic phosphodiesterase activity. Applicants note that the activity of SEQ ID NO:1 as a cyclic nucleotide phosphodiesterase protein is not at issue and has been established by the teachings of the instant specification.

Moreover, those 90% variants of SEQ ID NO:2 which are degenerative variants of SEQ ID NO:2 and which also encode SEQ ID NO:1, are understood by one of skill in the art to have the structural characteristics of proteins having cyclic nucleotide phosphodiesterase activity.

Independent claim 3 recites:

> An isolated polynucleotide encoding a polypeptide selected from the group consisting of:
>
> a.) a polypeptide comprising the amino acid sequence of SEQ ID NO:1,
>
> b) a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1,
>
> c) a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, said fragment having cyclic nucleotide phosphodiesterase activity, and
>
> d) an immunogenic fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1, said immunogenic fragment is used to make an antibody which specifically binds to an isolated polypeptide selected from the group consisting of a), b) and c).

Independent claim 11 recites:

> An isolated polynucleotide selected from the group consisting of:
>
> a) a polynucleotide comprising the polynucleotide sequence of SEQ ID NO:2,
>
> b) a polynucleotide comprising a polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:2,

c) a polynucleotide complementary to a polynucleotide of a),
d) a polynucleotide complementary to a polynucleotide of b) and
e) an RNA equivalent of a)-d).

While the Examiner concedes that the Specification provides an adequate written description of SEQ ID NO:2 and SEQ ID NO:1, encoded by SEQ ID NO:2, she alleges that it lacks an adequate written description of the 90% polynucleotide variants and the 90% polypeptide variants because, "the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed." (Office Action of August 29, 2003 at page 5). Applicants strongly disagree with this position.

Such a position ignores that the polynucleotides recited in claims 11 and 3 ***are*** described in terms of their ***structure***. That is, the polynucleotide variants recited in claim 11 (b) are "***at least 90% identical to the polynucleotide sequence of SEQ ID NO:***2." Additionally, the polypeptides recited in claim 3 (b) ***are*** described in terms of their ***structure***, i.e., the claimed polypeptide variants are "***at least 90% identical to the amino acid sequence of SEQ ID NO:***1." The structures of SEQ ID NO:2 and SEQ ID NO:1 are provided in the specification, for example, at pages 54-56 of the Sequence Listing and Figures 1A, 1B, 1C, 1D, 1E, and 1F. The phrases "percent identity" or "% identity" as well as methods for determining such identity are well known to the skilled artisan.

Applicants submit that this description is sufficient to describe the claimed genus of polynucleotides and the claimed genus of polypeptides based on the disclosure of the single species of polynucleotide, SEQ ID NO:2 and based on the disclosure of the single species of polypeptide, SEQ ID NO:1, for reasons stated in the USPTO's own training materials for implementation of the Written Description Guidelines under 35 USC § 112, first paragraph.

In the "Synopsis of Application of Written Description Guidelines" (USPTO Website www.uspto.gov, March 1, 2000), at page 53 of these guidelines, a claim to "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B" is considered to meet the written description requirements because:

> --- procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify all other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art.

The Guidelines further state:

> The single species disclosed (SEQ ID NO:3) is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity.

Thus, Applicants submit that just as variants of polypeptides which are at least 95% identical to a given species, i.e., SEQ ID NO:1 in the instant application, meet the USPTO's own Written Description Guidelines, so too do polypeptide variants at least 90% identical to SEQ ID NO:1 fulfill the USPTO's own Written Description Guidelines. Moreover, Applicants assert that such a guideline also supports the variants of polynucleotides which are at least 90% identical to SEQ ID NO:2. Therefore, the specification, as filed does indeed provide adequate written description support for a polypeptide having at least 90% sequence identity to SEQ ID NO:1.

A detailed description of the chemical and structural features of SEQ ID NO:2 which contribute to the characterization of SEQ ID NO:2 and other related polynucleotides which may encode members of the nucleotide phosphodiesterase gene family are provided, for example, at p. 56 of the Sequence Listing and Figures 1A-1F. Ninety percent variants of the claimed polynucleotides are described, for example, at p. 17, lines 3-9. Likewise, a detailed description of the chemical and structural features of SEQ ID NO:1 which contribute to the characterization of SEQ ID NO:1 and other related proteins related to the nucleotide phosphodiesterase gene family are provided, for example, at p. 15 line 16 to p. 16 line 25, pp. 54-56 of the Sequence Listing, and Figures 2A, 2B, 2C and 2D. Ninety percent variants of the claimed polypeptides are described, for example, at p. 16, lines 26-29.

When provided with the description as noted above, one of ordinary skill in the art "would have understood the inventor to be in possession of the claimed invention at the time of filing." That is, one of ordinary skill in the art would recognize polynucleotide and polypeptide sequences which are variants at least 90% identical to SEQ ID NO:2 and SEQ ID NO:1, respectively. Given a polynucleotide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO:2 and to determine the percent identity to SEQ ID NO:2 of the variant. Likewise, given a polypeptide sequence, it would be routine for one of skill in the art to recognize whether it was a variant

of SEQ ID NO:1, and to determine the percent identity to SEQ ID NO:1 of the variant. Accordingly, the specification provides an adequate written description of the recited variants of SEQ ID NO:2 and the recited variants of SEQ ID NO:1. That is, the polynucleotide sequences which are variants at least 90% identical to SEQ ID NO:2 and polypeptide sequences which are variants at least 90% identical to SEQ ID NO:1, respectively.

B. The specification provides an adequate written description as required by law

Applicants submit that case law in the area of the written description requirement of 35 U.S.C. 112, first paragraph is clear with regard to the details considered sufficient to describe a claimed genus:

> . . . Mention of representative compounds encompassed by generic claim language ***clearly is not required by Section 112 or any other provision of the statute***. But, where no explicit description of a generic invention is to be found in the specification . . . mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]

> . . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, ***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'*** *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

The specification sets forth a description of the claimed polynucleotide variants using "other appropriate language" as indicated above in connection with the remarks regarding a polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:2". The claimed variants have been described in terms of their relationship to the chemical structure of SEQ ID NO:2, their structural requirements at, for example, p. 56 of the Sequence Listing; and Figures 1A, 1B, 1C, 1D, 1E, and 1F and in terms of the structural motifs characteristic of cyclic phosphodiesterase proteins (specification, page 15, lines 19-29, as illustrated in Figures 1C, 1D, and 1E). The specification provides a means of identifying functional variants having 90% sequence identity with SEQ ID NO:1 at, for example, p. 17, lines 3-17 and the assay taught in Example X. Applicants therefore submit that the

"genus is sufficiently identified in [the instant] application by 'other appropriate language'" as stated in *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960). Thus, the polynucleotides of claims 3 and 11 constitute a limited, well-described genus.

Variants of SEQ ID NO:2 are defined in the Specification at, for example, at page 17, lines 3-9. The present application is directed, *inter alia*, to polynucleotides encoding PDE proteins, including polynucleotides encoding PDE9A related to the amino acid sequence of SEQ ID NO:1. The skilled artisan is aware that due to the degeneracy of the genetic code, there are alternative codons which when present in sequence variants of the polynucleotide sequence of SEQ ID NO:2 would still encode a polypeptide comprising the amino acid sequences of SEQ ID NO:1 and the polypeptide would have the cyclic nucleotide phosphodiesterase activity. For example, the amino acid" histidine" is encoded by either the codon "CAU" or "CAC", a change at the third position of the codon, either "U" or "C" does not alter the amino acid for which it encodes. Likewise, the amino acid "leucine"can be encoded by "UUA," "UUG," "CUU," "CUC," "CUA," and "CUG," where only the second position of the codon is invariant. Thus, one skilled in the art is well versed in the degeneracy of the genetic code.

Furthermore, the specification sets forth a description of the claimed polypeptide variants using "other appropriate language" as indicated above in connection with the remarks regarding an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1". The claimed variants have been described in terms of their relationship to the chemical structure of SEQ ID NO:1 and structural requirements at, for example, pp. 54-56 of the Sequence Listing; Figures 1A, 1B, 1C, 1D, 1E, and 1F; p. 15 line 16 to page 16 line 25 and Figures 2A, 2B, 2C and 2D. The specification provides a means of identifying functional variants having 90% sequence identity with SEQ ID NO:1 at, for example, p. 16, lines 26-29.

Applicants therefore submit that the polynucleotide variants and polypeptide variants each comprise a genus which "is sufficiently identified in [the instant] application by 'other appropriate language'" as stated in *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960). Furthermore, Applicants submit that "a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing" as stated in the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001. Accordingly, Claims 3, 6-8 and 11 meet the statutory requirements for

written description under 35 U.S.C. 112, first paragraph.

C. Conclusion

The Office Action failed to base its written description inquiry pertinent to the present claims in view of their scope. In particular, the subject matter of the claims of the instant application is defined in terms of the chemical structure of SEQ ID NO:2 and SEQ ID NO:1. Chemical structure would certainly be regarded by one of ordinary skill in the art to provide sufficient detail for the identification of the relevant characteristics of the instantly claimed invention. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polynucleotides and the genus of polypeptides defined by the present claims is adequately described, as evidenced by specific passages of the specification as set forth above. Furthermore, the Examiner has applied to the subject application a written description standard that has no basis in the law.

For at least the above reasons it is believed that Claims 3, 6-8 and 11 meet the written description requirement of 35 U.S.C. § 112, first paragraph. It is therefore requested that this rejection be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

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